UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,071	02/13/2002	David Bar-Or	4172-3-2	8825

22442 7590 07/25/2006

SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,071	BAR-OR ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *531-542,544-548 and 550-576* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *531-542,544-548 and 550-576* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20060217*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on April 20, 2006. Claims 543, and 549 have been cancelled. Claims 531-542, 544-548, and 550-576 are currently pending and are under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawal of Rejections

3. The rejection of claims 531, 532, 534-536, 541, 544, 545, and 569 under 35 U.S.C. 102(b) as being anticipated by Lane, T. et al. (Journal of Cell Biology, 125(4): 929-943 (1994)) is withdrawn.

Maintenance of Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 531-542, 544-548, and 550-576 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an angiogenic disease or condition by inhibiting angiogenesis using metal-binding peptides as disclosed in the examples and the declaration filed April 20, 2006, does not reasonably provide enablement for a method of

treating an angiogenic disease or condition with a metal-binding peptide encompassed by the formula, P_1-P_2; P_1 is Xaa_1 Xaa_2 His or Xaa_1 Xaa_2 His Xaa_3, the P_1 portion of the peptide is linear, P_2 is $(Xaa_4)_n$, where n is 0-10, and Xaa_1, Xaa_2, Xaa_3, and Xaa_4 are amino acids disclosed in claim 531. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was disclosed in the office action mailed September 30, 2005.

Response to Remarks

The declaration under 37 CFR 1.132 filed April 20, 2006 is insufficient to overcome the rejection of claims 531-542, 544-548, and 550-576 based upon 35 U.S.C. 112, first paragraph, scope of enablement as set forth in the last Office action because: the showing is not commensurate in scope of the claims.

Applicant's state several metal-binding peptides of the invention bind to copper and demonstrate the ability of these peptides to inhibit angiogenesis. Applicants describe the ability of peptides to inhibit the production of hydroxyl radicals caused by copper. Applicants describe experiments of the same peptides to inhibit the release of interleukin-8 (IL-8) from human umbilical vein endothelial cells (HUVECs). Applicants state IL-8 is a potent promoter of angiogenesis, and the results of the experiments provide evidence that the metal-binding peptides of the invention have the ability to inhibit angiogenesis. Applicants state that 27/32 of the peptides inhibited HUVEC proliferation, and that proliferation of endothelial cells is the first stage of angiogenesis, therefore the results provide evidence that the metal-binding peptides of the invention have the ability to inhibit angiogenesis. Applicants describe experiments of eleven

peptides that have copper binding stability constants as an indication that the peptides of the invention bind copper well. Applicant's tested nine peptides in the chicken egg chorioallantoic membrane assay, an art recognized in vivo assay for angiogenesis.

Applicant's arguments filed April 20, 2006 have been fully considered but they are not persuasive. The issue in this application is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable (see particularly section 3.) and 7.) in scope of enablement rejection), and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, absent direction/guidance regarding whether the peptide can tolerate the modifications contemplated a non-functional protein may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. In addition, figures D-H, S, and V of the declaration describe peptides with Gly in position Xaa_2, which is no longer encompassed by the pending claims.

New Rejections

Claim Rejections - 35 USC § 112

6. Claims 559-562, and 567 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 559-562 are improperly dependent claims, because they fail to further limit the peptide of claim 531. In particular for claim 561, the first diagram of a peptide has the Xaa_1 encompassing more than the recited amino acids from claim 531. R_1 in claim 561 describes alkyl, aryl, or heteroaryl derivatives in position Xaa_1.

8. Claim 567 recites a peptide. There is insufficient antecedent basis for this limitation in the claim. Particularly in claim 567, it is unclear how to distinguish the metal binding peptides? Suggest identifying a first metal binding peptide and a second metal binding peptide.

Claim Rejections - 35 USC § 102

9. Claims 531-542, 544-548, and 550-576 are rejected under 35 U.S.C. 102(b) as being anticipated by Hagiwara, D. et al. (JP 62-116565, IDS filed June 18, 2002, document 87).

Hagiwara et al. describe polypeptides Asp-Ala-His-Lys, and Thr-Leu-His-Arg, as medications to treat ulcers (see claim 1, and page 17, line 1 – page 18, line 20 of translated document). The peptide disclosed by Hagiwara et al. does describe the peptide currently being administered to an animal in the pending claims, and therefore would necessarily treat an angiogenic disease or condition.

Feit et al. (2003, J. Pat. Trade. Off. Soc., Vol. 85, No. 1, pages 5-21) teach three criteria for inherency. (1) The most important criterion is certainty. Citing *In re Tomlinson* and *In re Zierden*, Feit et al. state that certainty is established when the reference process necessarily **results** in the claimed process as opposed to a **possibility.** (2) The second criterion is chronology; it will always happen. Feit et al. state that the chronological test is forward chronology. Citing *Eli Lilly and Co. v Barr Laboratories, Inc.*, Feit et al. argue that the claimed result must always be obtained based upon the prior art method. 3) The third criterion is the legal standard. Feit et al., citing *Continental Can,* state that the legal standard is whether the missing descriptive material would be so recognized by a person of ordinary skill in the art as necessarily present in the thing. It is recognized by a person having ordinary skill in the art that structure of the polypeptide necessarily determines the function of the polypeptide.

Claim Rejections - 35 USC § 102/Claim Rejections - 35 USC § 103

10. Claims 531-542, 544-548, and 550-576 are rejected under 35 U.S.C. 102(b) as anticipated by Heavner et al. (WO 95/26744, IDS filed 2/17/2006, document AC) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Heavner et al. (WO 95/26744, IDS filed 2/17/2006, document AC) in view of Shimazawa et al. (Biol. Pharm. Bull. 22(2): 224-226 (1999)).

Heavner et al. describes the method of treating an animal suspected of suffering from a disease or disorder mediated by tumor necrosis factor-α activity comprising the step of administering to said individual a therapeutically effective amount of a peptide that comprises an amino acid sequence which consists of 4 to 25 amino acids and which inhibits tumor necrosis

factor-α activity, wherein said peptide comprises at least four amino acid residue fragment of a Markush group of peptides (see page 80, claim 27). Applicant is referred to SEQ ID NO: 58 and SEQ ID NO: 76, which describes peptides with His in position 3 of the polypeptide sequence.

Shimazawa et al. describes the antiangiogenic activity of tumor necrosis factor-α inhibitors derived from thalidomide (see entire document, particularly 4th, and 5th paragraphs, and Table 1).

Thus, it would have been obvious to the person having ordinary skill in the art to treat an angiogenic disease or disorder using the tumor necrosis factor-α inhibitor peptides as described by Heavner et al., because Shimazawa et al. have described the art recognized antiangiogenic activity of tumor necrosis factor-α inhibitors.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

July 17, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER